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(54) **HIGHLY-MINERALIZED OSTEOGENIC SPONGE COMPOSITIONS, AND USES THEREOF**

HOCHMINERALISIERTE OSTEOGENE SCHWAMMZUSAMMENSETZUNGEN UND IHRE
VERWENDUNG

COMPOSITIONS SPONGIEUSES OSTEOGENIQUES EXTREMEMENT MINERALISEES ET
LEURS UTILISATIONS

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(73) Proprietor: **SDGI Holdings, Inc.**
Wilmington, DE 19801 (US)

(72) Inventor: **MCKAY, William, F.**
Memphis, TN 38133 (US)

(74) Representative: **Allman, Peter John et al**
MARKS & CLERK,
Sussex House,
83-85 Mosley Street
Manchester M2 3LG (GB)

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Description**REFERENCE TO RELATED APPLICATION****FIELD OF THE INVENTION**

[0001] The present invention relates generally to osteogenic compositions. Specifically, the present invention relates to an osteogenic sponge composition effective for the induction of new bone growth in animals.

BACKGROUND OF THE INVENTION

[0002] Bone grafting has been commonly used to augment healing in the treatment of a broad range of musculoskeletal disorders. This procedure has several disadvantages. If the bone material is obtained from donors of the same species, such as an allograft, an increased risk of disease transmission and immune reaction exists. Bone material surgically removed from the patient, known as an autograft, is also undesirable because a sufficient amount of autogenous bone may not be available and the additional surgery necessary to obtain the autograft increases the risk of infection.

[0003] Due to the need for safer bone graft materials, efforts have been directed to finding bone graft substitutes. Candidate compositions include collagen and a bioceramic, such as hydroxyapatite, as these components are the chief structural materials in bone tissue. Bioceramics provide a porous matrix which encourages some new bone growth but, when used in powdered form, give rise to foreign body-giant cell reactions. Other compositions include demineralized bone powder and collagen. The osteogenic potential of these compositions have been found to be less than satisfactory.

[0004] The discovery of osteogenic factors and their application to bone graft substitute compositions has increased the effectiveness of the above-mentioned compositions. Although many preparations purport to be effective in bone repair in vertebrates, including higher animals such as primates, most of the experimentation done with the compositions have involved lower animals, such as mice and rats.

[0005] In light of this background, there remains a need for improved osteogenic compositions and methods that effectively induce bone growth in higher animals, including primates.

SUMMARY OF THE INVENTION

[0006] The invention provides in one preferred embodiment an osteogenic sponge composition useful for the induction of new bone growth in a mammal. This composition includes a resorbable sponge matrix material and an osteogenic factor, preferably one that preferably stimulates osteoblasts and osteoclasts, said osteogenic factor incorporated in the sponge matrix material. The resorbable sponge matrix material is desirably

a three-dimensionally stable yet flexible material, facilitating its use as an implant. The osteogenic factor is usually incorporated in an amount that causes an increased rate of resorption of said sponge matrix material in a mammal. The composition also includes a particulate mineral having an average particle diameter of at least about 0.5 mm embedded in the resorbable sponge matrix material, wherein the particulate mineral present in a weight ratio of at least 4:1 relative to the resorbable sponge matrix material so as to provide a scaffold for bone ingrowth in the presence of the osteogenic factor. More preferred compositions are even more highly mineralized, for example wherein the particulate mineral is present in a weight ratio of at least about 10:1 relative to the resorbable sponge matrix material. The particulate mineral is desirably formed of a synthetic calcium phosphate ceramic or of bone, especially cortical bone. The osteogenic factor is most preferably BMP-2 or LMP, or comprises a nucleotide sequence encoding BMP-2 or LMP.

[0007] Another embodiment of the present invention provides the use of an osteogenic sponge composition having a resorbable sponge matrix material and an osteogenic factor that stimulates osteoblasts and osteoclasts incorporated in the sponge matrix material in an amount that causes an increased rate of resorption of the sponge matrix material in the primate for the manufacture of a medicament for inducing bone growth in a primate. Particulate mineral having an average particle diameter of at least about 0.5 mm is embedded in said resorbable sponge matrix material and present in a weight ratio of at least 4:1 relative to the resorbable sponge matrix material, so as to provide a scaffold for bone ingrowth in the presence of the osteogenic factor. This osteogenic sponge composition is to be implanted in the primate in a void in which bone growth is desired, with the osteogenic sponge composition providing a scaffold for a duration sufficient for osteoid ingrowth through the void. Particularly preferred uses involve bone ingrowth to attain spinal fusions in humans.

[0008] Another preferred embodiment of the invention provides an osteogenic sponge composition effective for the induction of new bone growth in a mammal (especially a primate) that includes

a carrier consisting essentially of a resorbable sponge matrix with particulate mineral embedded in the resorbable sponge matrix, wherein the particulate mineral is present in an amount constituting at least about 95% by weight of the carrier. An osteogenic factor that stimulates osteoblasts and osteoclasts is incorporated in said carrier.

[0009] A still further aspect of the invention provides a highly mineralized sponge implant device consisting essentially of a resorbable sponge matrix formed of collagen and having particulate biocompatible mineral embedded within said matrix. In this embodiment, the device is comprised 1% to 3% by weight of the collagen and 97% to 99% by weight of the particulate biocompat-

ible mineral. In another inventive feature, an osteogenic factor can be incorporated in such an implant.

[0010] A further embodiment of the invention provides an interbody spinal fusion device that includes a load bearing member sized for insertion between adjacent vertebrae and any one of the aforementioned compositions retained by the load bearing member. Such fusion devices can be used in inventive interbody spinal fusion methods mammals, wherein the devices are to be appropriately implanted to facilitate spinal fusion.

[0011] A particular feature of the present invention relates to the discovery that the inclusion of an osteogenic factor, especially an osteoblast- and osteoclast-stimulating osteogenic factor, in a resorbable sponge composition causes a substantially accelerated resorption of the sponge. This rapid resorption can diminish or eliminate the capacity of the sponge composition to effectively stimulate and support new bone formation in a void filled with the sponge composition. This is particularly the case in primates, including humans, in which the rate of new bone formation is relatively slow. Objects of the present invention are to provide osteogenic sponge compositions effective for the induction of bone growth in mammals, particularly primates, including humans, and related methods and devices. These and other objects and advantages of the present invention will become apparent upon reading the descriptions herein.

BRIEF DESCRIPTION OF THE FIGURES

[0012]

FIGs. 1 and 2 depict a digitized images of computerized tomography (CT) scans of an L4-L5 posterolateral spinal fusions performed on rhesus monkeys as described in Example 5 (top panels, section through superior transverse processes; middle panels, section through disc space; lower panels, section through inferior transverse processes).

DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0013] For the purposes of promoting an understanding of the principles of the invention, reference will now be made to preferred embodiments and specific language will be used to describe the same. It will nevertheless be understood that no limitation of the scope of the invention is thereby intended, such alterations and further modifications of the invention, and such further applications of the principles of the invention as illustrated herein, being contemplated as would normally occur to one skilled in the art to which the invention relates.

[0014] As described above, the invention relates in certain aspects to osteogenic sponge compositions effective for the induction of new bone growth in mammals and methods for inducing bone growth in mammals. The present invention features osteogenic sponge compo-

sitions effective for use in primates, wherein the compositions exhibit high osteoinductive potential and provide a lasting mineral scaffold to support bone ingrowth. Such preferred compositions include a porous, resorbable sponge carrier, such as collagen in sponge form, and an osteogenic factor that stimulates the action of both osteoblasts (which biologically facilitate the formation of bone) and osteoclasts (which biologically facilitate the resorption of bone). In accordance with the present invention, it has been found that the incorporation of an effective inductive amount of an osteogenic factor, such as a bone morphogenetic protein (BMP), stimulates osteoclasts to such a level that a porous resorbable carrier is quickly resorbed and, in the absence of a high mineral component in the composition, causes the performance of the composition to suffer in some cases to the extent that the observation of substantial bone ingrowth is sporadic. Although such non-mineralized sponge compositions may be highly effective for repair of bone defects in lower animals, such as mice, that have a faster bone growth rate, they are less effective in large animals such as primates, including humans.

[0015] Accordingly, a feature of the present invention is the provision of an osteogenic composition in the form of a sponge that includes a substantial amount of a relatively slowly-resorbed mineral component that remains at the implant site after the carrier has been rapidly resorbed, in order to provide a scaffold for new bone formation that is not prematurely resorbed due to the osteoclastic potentiation by the bone morphogenetic protein in the composition. The present invention also provides uses of such osteogenic compositions in the manufacture of a medicament for the treatment of bone trauma, disease and defects, for artificial arthrodeses and for other treatment where new bone formation is desired, especially in primates, including humans.

[0016] The sponge matrix material is preferably collagenous. A wide variety of collagen materials are suitable for the sponge matrix. Naturally occurring collagens may be subclassified into several different types depending on their amino acid sequence, carbohydrate content and presence or absence of disulfide crosslinks. Types I and III collagen are two of the most common subtypes of collagen. Type I collagen is present in skin, tendon and bone whereas Type III collagen is found primarily in skin. The collagen in the composition may be obtained from skin, bone, tendon, or cartilage and purified by methods known in the art. Alternatively, the collagen may be purchased commercially. The collagen in the composition is preferably Type I bovine collagen.

[0017] The collagen carrier can further be atelopeptide collagen and/or telopeptide collagen. Moreover, both non-fibrillar and fibrillar collagen may be used. Non-fibrillar collagen is collagen that has been solubilized and has not been reconstituted into its native fibrillar form.

[0018] The sponge carrier may also be formed of oth-

er natural or synthetic polymeric materials, in addition to or as an alternative to collagen. For example, the sponge carrier may be formed of gelatin (e.g. foamed gelatin), in addition collagen or as an alternative to collagen. Other natural and synthetic polymers are also known for the formation of biocompatible sponge materials, and can be used herein.

[0019] As indicated above, preferred compositions of the invention also include an osteoinductive factor, such as an osteoinductive protein or a nucleotide sequence encoding an osteoinductive protein operably associated with a promoter (e.g. provided in a vector such as a viral vector) which drives expression of the gene in the animal recipient to produce an effective amount of the protein. The osteogenic factor utilized in the present invention can be one that stimulates production or activity of osteoblasts and osteoclasts. The factor is preferably a bone morphogenetic protein (BMP) or a LIM mineralization protein (LMP), or comprises a nucleotide sequence encoding a BMP or LMP. Recombinant human BMPs are preferred, and may be commercially obtained or prepared as described and known in the art, e.g. in U.S. Patent Nos. 5,187,076 to Wozney et al.; 5,366,875 to Wozney et al.; 4,877,864 to Wang et al.; 5,108,932 to Wang et al.; 5,116,738 to Wang et al.; 5,013,649 to Wang et al.; 5,106,748 to Wozney et al.; and PCT Patent Nos. WO93/00432 to Wozney et al.; WO94/2693 to Celeste et al.; and WO94/26892 to Celeste et al. Further, the osteoinductive factor may be isolated from bone. Methods for isolating BMP from bone are described in U.S. Patent no. 4,294,753 to Urist and Urist et al., PNAS 371, 1984. Recombinant human BMP-2 (rhBMP-2), recombinant human BMP-4 (rhBMP-4), recombinant human BMP-7 (rhBMP-7) or heterodimers thereof are most preferred. The osteoinductive factor may also be LIM mineralization protein (LMP) or a suitable vector incorporating a gene encoding the same operably associated with a promoter, as described in WO99/06563 (see also genbank accession No. AF095585). When such vectors are employed as osteogenic factors in accordance with the invention, they are preferably delivered in conjunction with cells, for example autologous cells from the recipient of the implant. Most preferably the vector is delivered in conjunction with autologous white blood cells derived from bone marrow or peripheral blood of the recipient. These cells may be applied to the sponge composition along with the osteogenic factor prior to implantation.

[0020] The particulate mineral component includes a natural or synthetic mineral that is effective in providing a scaffold for bone ingrowth as the resorbable carrier is resorbed. The mineral may be, for example, bone, especially cortical bone, or a synthetic bioceramic such as a biocompatible calcium phosphate ceramic. Illustrative ceramics include tricalcium phosphate, hydroxyapatite, and biphasic calcium phosphate. These mineral components may be purchased commercially or obtained or synthesized by methods known in the art.

[0021] Biphasic calcium phosphate is a particularly preferred synthetic ceramic for use in the invention. Desirably, such biphasic calcium phosphate will have a tricalcium phosphate:hydroxyapatite weight ratio of about 50:50 to about 95:5, more preferably about 70:30 to about 95:5, even more preferably about 80:20 to about 90:10, and most preferably about 85:15.

[0022] In general, the amount of mineral in the osteogenic sponge composition must be sufficient to provide a scaffold that will remain in the patient for a period of time sufficient for the formation of osteoid in the void for which bone growth is desired. Typically, this period of time will be about 6 to about 8 weeks. The minimum level of mineral that must be present in the composition is also dependent on the activity of the BMP in the composition; the higher the activity of the BMP, the greater the content of the mineral matrix required to counter the osteoclastic potentiation of the BMP. The rate of resorption of the resorbable carrier also increases as the BMP concentration increases.

[0023] In preferred aspects of the invention, the particulate mineral:resorbable sponge matrix weight ratio will be at least about 4:1, more preferably at least about 10:1. In particularly preferred sponge implants, the particulate mineral will constitute at least 95% by weight of the sponge implant. For example, highly effective sponge carrier devices are provided wherein they comprise about 97% to about 99% by weight particulate mineral and about 1% to about 3% of the collagen or other sponge-forming matrix material. Moreover, it is preferred that the mineral component have an average particle size of at least about 0.5 mm, more preferably about 0.5 mm to about 5 mm, and most preferably about 1 mm to about 3 mm.

[0024] To make the sponge implant, a collagen slurry may be formed as known and preferably is chilled to increase its viscosity to help suspend the porous particulate mineral component. The porous particulate mineral is dispersed into the collagen slurry and gently mixed. After the porous particulate mineral component is uniformly dispersed in the slurry, the slurry is poured into sterile trays or other forms and freeze dried. The sheets of composite sponge are then removed from the freeze drier and exposed to a glutaraldehyde cross-linking agent. The composite sponge formed is generally three-dimensionally stable and can be sterilized and packaged in accordance with known procedures.

[0025] The dimensions of the sponge produced may vary depending on the application. Dimensions of a typical sponge are, for example, about 10 cm (length) x 7.5 cm (width) x 0.35 cm (height).

[0026] As one example, BMP or other osteogenic factors may be included in the formed sponge by combining the BMP with a liquid carrier as known in the art and infusing the liquid into the sponge.

[0027] As further enhancements of the compositions of the present invention, those skilled in the art will readily appreciate that other osteogenic enhancing factors

may be incorporated into the composition. Such additional factors include host compatible osteogenic progenitor cells, autographic bone marrow, allographic bone marrow, transforming growth factor- β , fibroblast growth factor, platelet-derived growth factor, insulin-like growth factor, microglobulin- β , antibiotics and steroids.

[0028] In yet another aspect of the invention, the use of the above-described osteogenic sponge composition is provides for the manufacture of a medicament for inducing bone growth in mammals. The composition is to be implanted at a site at which bone growth is desired, e.g., to treat a disease, defect or location of trauma, and/or to promote artificial arthrodesis. The hydrated sponge composition may be rolled up prior to packing the sponge into the implantation site.

[0029] Once in place, the osteogenic sponge composition will effectively induce and support ingrowth of bone into the desired area even in a primate such as a human that exhibits a relatively slow rate of bone formation compared to smaller mammals, such as rodents or rabbits. Although the collagen carrier is resorbed relatively quickly, the substantial mineral component remains as a scaffolding to support new bone growth in and through the desired area.

[0030] The above osteogenic sponge compositions of the present invention are especially advantageous when used in bones or bone portions that exhibit only low to moderate vascularization. Such low to moderate vascularized regions exhibit low rates of bone formation so rapid resorption of a carrier poses a problem. Examples of low to moderate vascularized sites include, for example, transverse processes or other posterior elements of the spine.

[0031] An especially preferred use of the sponge compositions of the present invention is as an implant to promote arthrodesis between vertebrae in spinal fusions in humans or other primates, including interbody, posterior and/or posterolateral fusion techniques. Although the rate of bone formation in the primate spine is relatively slow overall and thus will benefit generally from the present invention, the elements to be fused in posterior and posterolateral fusions exhibit particularly low levels of vascularization and thus fusions of these elements are expected to benefit markedly from the invention.

[0032] Moreover, the osteogenic sponge compositions can be incorporated with a load-bearing member used in a spinal fusion, including hollow spinal cages, dowels or other devices known in the art having a pocket, chamber or other mechanism for retaining the osteogenic sponge composition. The load-bearing member desirably will have a compressive strength of at least about 10,000 N. Suitable such load bearing members are described, for example in U.S. Patent Nos. 5522899, 5785710, 5776199 and 5814084.

[0033] Reference will now be made to specific examples using the processes described above. It is to be understood that the examples are illustrative and not

limiting of the invention.

EXAMPLE 1

PREPARATION OF COLLAGEN SPONGE/BONE PARTICLE COMPOSITE

[0034] 12 grams of deproteinized cortical bone chips, 1-3 mm in size, were added to 12 grams of collagen slurry (0.192 grams of collagen). This composite slurry was poured into a 7.5 cm x 10.0 cm mold, freeze dried, double sterile packaged, and sterilized by ETO gas sterilization.

EXAMPLE 2

PREPARATION OF COLLAGEN SPONGE/ SYNTHETIC CERAMIC COMPOSITE

[0035] 12 grams of biphasic calcium phosphate particles, 1 mm in diameter, were added to 12 grams of collagen slurry (0.192 grams of collagen). This composite slurry was poured into a 7.5 cm x 10.0 cm mold, freeze dried, double sterile packaged, and sterilized by ETO gas sterilization.

EXAMPLE 3

PREPARATION OF COLLAGEN SPONGE/BONE PARTICLE COMPOSITE

[0036] 12 grams of deproteinized cortical bone chips, 1-3 mm in size, were added to 24 grams of collagen slurry (0.192 grams of collagen). This composite slurry was poured into a 7.5 cm x 10.0 cm mold, freeze dried, double sterile packaged, and sterilized by ETO gas sterilization.

EXAMPLE 4

PREPARATION OF COLLAGEN SPONGE/ SYNTHETIC CERAMIC COMPOSITE

[0037] 12 grams of biphasic calcium phosphate particles, 1 mm in diameter, were added to 24 grams of collagen slurry (0.192 grams of collagen). This composite slurry was poured into a 7.5 cm x 10.0 cm mold, freeze dried, double sterile packaged, and sterilized by ETO gas sterilization.

EXAMPLE 5

L4-L5 POSTEROLATERAL INTERTRANSVERSE PROCESS SPINAL FUSION STUDY

[0038] The present study was performed to determine the effect of the osteogenic sponge compositions of the present invention on spinal fusion.

[0039] The experimental group included two adult rhesus monkeys (*Macaca mulatta*). The monkeys were anesthetized with 3-5 mg/kg telazol intramuscularly (i. m.). The anesthesia was maintained with 1.5-2.0% isoflurane. After anesthesia was achieved, animals were shaved, prepared with betadine and sterily draped. The surgical site was infiltrated with 10-15 ml of 0.25% marcaine to aid with immediate postoperative analgesia. A midline posterior skin incision was made over the lumbar spine. The paraspinal muscles were reflected using elevators, exposing the lamina and the transverse processes of the L4 and L5 vertebral bodies. The transverse processes of the two vertebrae to be fused were debrided with an electric burr.

[0040] Composite sponges, having dimension of 3.5 cm x 1.4 cm x 0.35 cm, were prepared using techniques as described in Examples 1 and 2. The sponges included, on a weight basis, 97% biphasic calcium phosphate (15% hydroxyapatite and 85% tricalcium phosphate, 1 mm particle size) and 3% collagen. Recombinant human BMP-2 (rhBMP-2) was prepared at a concentration of 3.0 mg/ml in a buffered solution. Each sponge was infused with 1.5 ml of the rhBMP-2 solution.

[0041] The sponges were placed in the paraspinal bed directly on top of and bridging the two adjacent transverse processes. The sponges were placed bilaterally, with two sponges (one on top of the other) on each side of the spine, resulting in a total dose of 9 mg rhBMP-2 per implant site. The animals were allowed to recover and move around ad libitum without restrictions during the study period.

[0042] The spines were manually assessed for fusion upon sacrifice (2, 4 and 6 months) and determined to be fused based upon the absence of motion during attempted bending, and presence of histological bridging bone.

[0043] The fusions were also evaluated by CT scan at 2, 4 and 6 months after implantation. FIGS. 1 and 2 show the CT scans for each subject studied. FIGS. 1 and 2 demonstrate the sequence of events that occur within the composite sponge carrier loaded with rhBMP-2. On the far left of the figures are three CT sections equally spaced throughout the fusion mass at 2 months post-operative, showing that resorption of the composite sponge is just about complete due to the lack of radiopacity of the ceramic granules. The three middle CT sections show these same three CT sections at four months with increased bone deposition where the carrier once resided. The composite sponge has maintained the space within the soft tissue site for a sufficient enough period of time for the desired volume of new bone deposition to occur. Finally, the far right three CT scans show even further bone deposition, remodeling and maturation with the formation of outer cortices around the periphery of the fusion masses by six months.

Claims

1. An osteogenic sponge composition useful for the induction of new bone growth in a mammal, comprising:
 - a resorbable sponge matrix material;
 - an osteogenic factor, said osteogenic factor incorporated in said sponge matrix material in an amount that causes an increased rate of resorption of said sponge matrix material in a mammal; and
 - particulate mineral having an average particle diameter of at least 0.5 mm embedded in said resorbable sponge matrix material, said particulate mineral present in a weight ratio of at least 4:1 relative to said resorbable sponge matrix material, so as to provide a scaffold for bone ingrowth in the presence of said osteogenic factor.
2. The osteogenic sponge composition of claim 1, wherein said particulate mineral is present in a weight ratio of at least 10:1 relative to said resorbable sponge matrix material.
3. The osteogenic sponge composition of claim 1, wherein said osteogenic factor comprises a bone morphogenetic protein, a LIM mineralization protein, or a nucleotide sequence encoding a bone morphogenetic protein or a LIM mineralization protein.
4. The osteogenic sponge composition of claim 1, wherein said resorbable sponge matrix material includes collagen.
5. The osteogenic sponge composition of claim 3, wherein said resorbable sponge matrix material includes collagen.
6. The osteogenic sponge composition of claim 1, wherein said particulate mineral is selected from the group consisting of bone particles and biocompatible synthetic calcium phosphate ceramics.
7. The osteogenic sponge composition of claim 6, wherein said particulate mineral comprises biphasic calcium phosphate.
8. The osteogenic sponge composition of claim 7, wherein said biphasic calcium phosphate has a porosity of at least 50%.
9. The osteogenic sponge composition of claim 8, wherein said particulate mineral includes bone particles.

10. The osteogenic sponge composition of claim 9, wherein said bone particles are cortical bone particles.
11. The osteogenic sponge composition of claim 1, which is comprised at least 95% by weight of said particulate mineral.
12. The osteogenic sponge composition of claim 1, wherein said particulate mineral has an average particle size in the range of 0.5 mm to 5.0 mm.
13. The osteogenic sponge composition of claim 1, wherein said porous particulate mineral has an average particle size in the range of 1 to 2 mm.
14. The osteogenic sponge composition of claim 1, wherein said osteogenic factor is a bone morphogenetic protein.
15. The osteogenic sponge composition of claim 14, wherein said bone morphogenetic protein is a recombinant human protein.
16. The osteogenic sponge composition of claim 15, wherein said bone morphogenetic protein is BMP-2 or BMP-7.
17. The osteogenic sponge composition of claim 16, further comprising an osteogenic enhancing factor selected from the group consisting of autographic bone marrow, allographic bone marrow, transforming growth factor- β , fibroblast growth factor, platelet-derived growth factor, insulin-like growth factor, microglobulin- β , and steroids.
18. An osteogenic sponge composition effective for the induction of new bone growth in a primate, comprising:
 - a resorbable sponge matrix material; an osteogenic factor that stimulates osteoblasts and osteoclasts, said osteogenic factor incorporated in said sponge matrix material in an amount that causes an increased rate of resorption of said sponge matrix material in the primate; and
 - particulate mineral having an average particle diameter of at least 0.5 mm embedded in said resorbable sponge matrix material, said particulate mineral present in a weight ratio of at least 4:1 relative to said resorbable sponge matrix material, so as to provide a mineral scaffold for a duration sufficient for osteoid ingrowth through an area in which said sponge composition is implanted.
19. The sponge composition of claim 18 wherein the primate is a human.
20. The use of an osteogenic sponge composition comprising:
 - a resorbable sponge matrix material; an osteogenic factor that stimulates osteoblasts and osteoclasts, said osteogenic factor incorporated in said sponge matrix material in an amount that causes an increased rate of resorption of said sponge matrix material in the primate; and
 - particulate mineral having an average particle diameter of at least 0.5 mm embedded in said resorbable sponge matrix material, said particulate mineral present in a weight ratio of at least 4:1 relative to said resorbable sponge matrix material, so as to provide a scaffold for bone ingrowth in the presence of said osteogenic factor; for the manufacture of a medicament for inducing bone growth in a primate.
21. The use of claim 20, wherein said particulate mineral is present in a weight ratio of at least 10:1 relative to said resorbable sponge matrix material.
22. The use of claim 21, wherein said osteogenic factor comprises a bone morphogenetic protein, a LIM mineralization protein, or a nucleotide sequence encoding a bone morphogenetic protein or LIM mineralization protein.
23. The use of claim 20, wherein said resorbable sponge matrix material includes collagen.
24. The use of claim 22, wherein said resorbable sponge matrix material includes collagen.
25. The use of claim 20, wherein said particulate mineral is selected from the group consisting of bone, a synthetic biocompatible calcium phosphate ceramic, or a mixture thereof.
26. The use of claim 25, wherein said porous particulate mineral comprises biphasic calcium phosphate.
27. The use of claim 26, wherein said biphasic calcium phosphate has a porosity of at least 50%.
28. The use of claim 20, wherein said particulate mineral includes bone particles.
29. The use of claim 28, wherein said bone particles are cortical bone particles.
30. The use of claim 20, wherein said osteoinductive sponge composition is comprised at least 95% by

weight of said particulate mineral.

31. The use of claim 20, wherein said particulate mineral has an average particle size of 0.5 mm to 5.0 mm.

32. The use of claim 20, wherein said porous particulate mineral has an average particle size of 1 to 2 mm.

33. The use of claim 20, wherein said osteogenic factor is a bone morphogenetic protein.

34. The use of claim 33, wherein said bone morphogenetic protein is a recombinant human protein.

35. The use of claim 33, wherein said bone morphogenetic protein is BMP-2 or BMP-7.

36. The use of claim 20, wherein the primate is a human.

37. The use of claim 20, wherein the area is in the spine of said primate.

38. The use of claim 37, wherein the bone growth is induced to attain a spinal fusion.

39. The use of claim 38, wherein the spinal fusion is an interbody spinal fusion.

40. The use of claim 38, wherein the spinal fusion is a posterolateral spinal fusion.

41. The use of claim 38, wherein the spinal fusion includes a fusion between transverse processes of adjacent vertebrae.

42. An osteogenic sponge composition for the induction of new bone growth in a primate, comprising:

a carrier consisting essentially of a resorbable sponge matrix with particulate mineral embedded in said resorbable sponge matrix, said particulate mineral present in an amount constituting at least 95% by weight of said carrier; and an osteogenic factor.

43. A highly mineralized sponge implant device consisting essentially of a resorbable sponge matrix formed of collagen and having particulate biocompatible mineral embedded within said matrix, said device comprised 1% to 3% by weight of the collagen and 97% to 99% by weight of the particulate biocompatible mineral.

44. The device of claim 42 wherein the particulate biocompatible mineral comprises bone particles.

45. The device of claim 42 wherein the particulate biocompatible mineral includes a synthetic ceramic.

46. The device of claim 44 wherein the ceramic material includes a calcium phosphate ceramic.

47. The device of claim 45 wherein the calcium phosphate ceramic is biphasic calcium phosphate.

48. An osteogenic implant, comprising:

a resorbable matrix carrier comprised 1% to 3% by weight of collagen in sponge form and 97% to 99% by weight of a particulate biocompatible mineral embedded within said collagen; and an osteogenic factor.

49. An interbody spinal fusion device, comprising:

a load bearing member sized for insertion between adjacent vertebrae; and a composition according to any of claims 1-19 and 42-48 retained by said load bearing member.

50. The use of an interbody spinal fusion device according to claim 49, for the manufacture of a medical instrument for interbody spinal fusion in a mammal.

Patentansprüche

1. Osteogene Schwammzusammensetzung, die zur Induktion von neuem Knochenwachstum in einem Säuger nützlich ist, umfassend:

Ein resorbierbares Schwammatrix-Material;

einen osteogenen Faktor, wobei der osteogene Faktor in das Schwammatrix-Material in einer Menge eingebaut ist, die eine erhöhte Resorptionsrate des Schwammatrix-Materials in einem Säuger bewirkt; und

partikulären Mineralstoff mit einem durchschnittlichen Partikeldurchmesser von mindestens 0,5 mm, eingebettet in das resorbierbare Schwammatrix-Material, wobei der partikuläre Mineralstoff in einem Gewichtsverhältnis von mindestens 4:1 bezogen auf das resorbierbare Schwammatrix-Material vorliegt, um auf diese Weise ein Gerüst zum Einwachsen von Knochen in Gegenwart des osteogenen Faktors bereitzustellen.

2. Osteogene Schwammzusammensetzung nach Anspruch 1, worin der partikuläre Mineralstoff in einem Gewichtsverhältnis von mindestens 10:1 bezogen

- auf das resorbierbare Schwammatrix-Material vorhanden ist.
3. Osteogene Schwammzusammensetzung nach Anspruch 1, worin der osteogene Faktor ein Bone Morphogenetic Protein (knochenbildendes Protein), ein LIM-Mineralisationsprotein oder eine Nukleotidsequenz, kodierend ein Bone Morphogenetic Protein oder ein LIM-Mineralisationsprotein, umfasst.
 4. Osteogene Schwammzusammensetzung nach Anspruch 1, worin das resorbierbare Schwammatrix-Material Kollagen einschließt.
 5. Osteogene Schwammzusammensetzung nach Anspruch 3, worin das resorbierbare Schwammatrix-Material Kollagen einschließt.
 6. Osteogene Schwammzusammensetzung nach Anspruch 1, worin der partikuläre Mineralstoff aus der Gruppe ausgewählt ist, bestehend aus Knochenpartikeln und biokompatiblen synthetischem Calciumphosphat-Keramikmaterial.
 7. Osteogene Schwammzusammensetzung nach Anspruch 6, worin der partikuläre Mineralstoff biphasisches Calciumphosphat umfasst.
 8. Osteogene Schwammzusammensetzung nach Anspruch 7, worin das biphasische Calciumphosphat eine Porosität von mindestens 50 % aufweist.
 9. Osteogene Schwammzusammensetzung nach Anspruch 8, worin der partikuläre Mineralstoff Knochenpartikel einschließt.
 10. Osteogene Schwammzusammensetzung nach Anspruch 9, worin die Knochenpartikel Kortikalisknochenpartikel sind.
 11. Osteogene Schwammzusammensetzung nach Anspruch 1, die mindestens 95 Gew.-% des partikulären Mineralstoffs umfasst.
 12. Osteogene Schwammzusammensetzung nach Anspruch 1, worin der partikuläre Mineralstoff eine durchschnittliche Partikelgröße im Bereich von 0,5 mm bis 5,0 mm aufweist.
 13. Osteogene Schwammzusammensetzung nach Anspruch 1, worin der poröse partikuläre Mineralstoff eine durchschnittliche Partikelgröße im Bereich von 1 bis 2 mm aufweist.
 14. Osteogene Schwammzusammensetzung nach Anspruch 1, worin der osteogene Faktor ein Bone Morphogenetic Protein ist.
 15. Osteogene Schwammzusammensetzung nach Anspruch 14, worin das Bone Morphogenetic Protein ein rekombinantes humanes Protein ist.
 16. Osteogene Schwammzusammensetzung nach Anspruch 15, worin das Bone Morphogenetic Protein BMP-2 oder BMP-7 ist.
 17. Osteogene Schwammzusammensetzung nach Anspruch 16, die weiter einen osteogenen Enhancement-Faktor umfasst, der aus der Gruppe ausgewählt ist, bestehend aus autogenem Knochenmark, allogenen Knochenmark, transformierendem Wachstumsfaktor- β , Fibroblastenwachstumsfaktor, Plättchenwachstumsfaktor, insulinähnlichem Wachstumsfaktor, Mikroglobulin- β und Steroiden.
 18. Osteogene Schwammzusammensetzung, die zur Induktion von neuem Knochenwachstum in einem Primaten wirksam ist, umfassend:

Ein resorbierbares Schwammatrix-Material;

einen osteogenen Faktor, der Osteoblasten und Osteoklasten stimuliert, wobei der osteogene Faktor in das Schwammatrix-Material in einer Menge inkorporiert wird, die eine erhöhte Resorptionsrate des Schwammatrix-Materials in dem Primaten bewirkt; und

partikuläres Material mit einem durchschnittlichen Partikeldurchmesser von mindestens 0,5 mm, eingebettet in dem resorbierbaren Schwammatrix-Material, wobei der partikuläre Mineralstoff in einem Gewichtsverhältnis von mindestens 4:1 bezogen auf das resorbierbare Schwammatrix-Material vorliegt, um auf diese Weise ein Mineralstoffgerüst für eine Dauer bereitzustellen, die für das Einwachsen von Osteoid durch einen Bereich, in den die Schwammzusammensetzung implantiert ist, ausreichend ist.
 19. Schwammzusammensetzung nach Anspruch 18, worin der Primat ein Mensch ist.
 20. Verwendung einer osteogenen Schwammzusammensetzung, umfassend:

Ein resorbierbares Schwammatrix-Material;

einen osteogenen Faktor, der Osteoblasten und Osteoklasten stimuliert, wobei der osteogene Faktor in das Schwammatrix-Material in einer Menge inkorporiert wird, die eine erhöhte Resorptionsrate des Schwammatrix-Materials in den Primaten bewirkt; und

partikulären Mineralstoff mit einem durchschnittlichen Partikeldurchmesser von mindestens 0,5 mm, eingebettet in das resorbierbare Schwammatrix-Material, wobei der partikuläre Mineralstoff in einem Gewichtsverhältnis von mindestens 4:1 bezogen auf das resorbierbare Schwammatrix-Material vorhanden ist, um auf diese Weise ein Gerüst für das Einwachsen von Knochen in Gegenwart des osteogenen Faktors bereitzustellen;

zur Herstellung eines Medikamentes zur Induktion von Knochenwachstum in einem Primaten.

21. Verwendung nach Anspruch 20, worin der partikuläre Mineralstoff in einem Gewichtsverhältnis von mindestens 10:1 bezogen auf das resorbierbare Schwammatrix-Material vorhanden ist.
22. Verwendung nach Anspruch 21, worin der osteogene Faktor ein Bone Morphogenetic Protein, ein LIM-Mineralisationsprotein oder eine Nukleotidsequenz, kodierend ein Bone Morphogenetic Protein oder LIM-Mineralisationsprotein, umfasst.
23. Verwendung nach Anspruch 20, worin das resorbierbare Schwammatrix-Material Kollagen einschließt.
24. Verwendung nach Anspruch 22, worin das resorbierbare Schwammatrix-Material Kollagen einschließt.
25. Verwendung nach Anspruch 20, worin der partikuläre Mineralstoff aus der Gruppe ausgewählt ist, bestehend aus Knochen, einem synthetischen biokompatiblen Calciumphosphat-Keramikmaterial oder einem Gemisch davon.
26. Verwendung nach Anspruch 25, worin der poröse, partikuläre Mineralstoff biphasisches Calciumphosphat umfasst.
27. Verwendung nach Anspruch 26, worin das biphasische Calciumphosphat eine Porosität von mindestens 50 % aufweist.
28. Verwendung nach Anspruch 20, worin der partikuläre Mineralstoff Knochenpartikel einschließt.
29. Verwendung nach Anspruch 28, worin die Knochenpartikel Kortikalisknochenpartikel sind.
30. Verwendung nach Anspruch 20, worin die osteoinduktive Schwammzusammensetzung mindestens 95 Gew.-% des partikulären Mineralstoffs enthält.
31. Verwendung nach Anspruch 20, worin der partiku-

läre Mineralstoff eine durchschnittliche Partikelgröße von 0,5 mm bis 5,0 mm aufweist.

32. Verwendung nach Anspruch 20, worin der poröse partikuläre Mineralstoff eine durchschnittliche Partikelgröße von 1 bis 2 mm aufweist.
33. Verwendung nach Anspruch 20, worin der osteogene Faktor ein Bone Morphogenetic Protein ist.
34. Verwendung nach Anspruch 33, worin das Bone Morphogenetic Protein ein rekombinantes humanes Protein ist.
35. Verwendung nach Anspruch 33, worin das Bone Morphogenetic Protein BMP-2 oder BMP-7 ist.
36. Verwendung nach Anspruch 20, worin der Primat ein Mensch ist.
37. Verwendung nach Anspruch 20, worin sich der Bereich in der Wirbelsäule des Primaten befindet.
38. Verwendung nach Anspruch 37, worin das Knochenwachstum zum Erreichen einer Spinalfusion induziert wird.
39. Verwendung nach Anspruch 38, worin die Spinalfusion eine interkorporelle Spinalfusion darstellt.
40. Verwendung nach Anspruch 38, worin die Spinalfusion eine posterolaterale Spinalfusion darstellt.
41. Verwendung nach Anspruch 38, worin die Spinalfusion eine Fusion zwischen Querfortsätzen benachbarter Wirbel einschließt.
42. Osteogene Schwammzusammensetzung zur Induktion von neuem Knochenwachstum in einem Primaten, umfassend:

Einen Träger, im Wesentlichen bestehend aus einem resorbierbaren Schwammatrix-Material mit partikulärem Mineralstoff in die resorbierbare Schwammatrix eingebettet, wobei der partikuläre Mineralstoff in einer Menge vorhanden ist, die mindestens 95 Gew.-% des Trägers ausmacht; und

einen osteogenen Faktor.
43. Hochmineralisierte Schwammimplantatvorrichtung, bestehend im Wesentlichen aus einer resorbierbaren Schwammatrix, gebildet aus Kollagen und mit partikulärem biokompatiblen Mineralstoff in der Matrix eingebettet, wobei die Vorrichtung 1 Gew.-% bis 3 Gew.-% des Kollagens und 97 Gew.-% bis 99 Gew.-% des partikulären biokompatiblen

Mineralstoffs umfasst.

44. Vorrichtung nach Anspruch 42, worin der partikuläre biokompatible Mineralstoff Knochenpartikel umfasst. 5
45. Vorrichtung nach Anspruch 42, worin der partikuläre biokompatible Mineralstoff ein synthetisches Keramikmaterial einschließt. 10
46. Vorrichtung nach Anspruch 44, worin das Keramikmaterial ein Calciumphosphat-Keramikmaterial einschließt.
47. Vorrichtung nach Anspruch 45, worin das Calciumphosphat-Keramikmaterial biphasisches Calciumphosphat darstellt. 15
48. Osteogenes Implantat, umfassend:
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Einen resorbieren Matrixträger, umfassend 1 Gew.-% bis 3 Gew.-% Kollagen in Schwammform und 97 Gew.-% bis 99 Gew.-% eines partikulären biokompatiblen Mineralstoffs, eingebettet in das Kollagen; und 25
einen osteogenen Faktor.
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49. Interkorporelle Spinalfusionsvorrichtung umfassend:
Ein tragfähiges Glied, größtmäßig abgemessen zum Einsatz zwischen benachbarten Wirbeln; und 35
eine Zusammensetzung nach einem der Ansprüche 1 - 19 und 42 - 48, die durch das tragfähige Glied zurückgehalten wird. 40
50. Verwendung einer interkorporellen Spinalfusionsvorrichtung nach Anspruch 49, zur Herstellung eines Medikamentes zur interkorporellen Spinalfusion in einem Säuger. 45

Revendications

1. Une composition spongieuse à activité ostéogénique utile dans l'induction d'une nouvelle croissance osseuse chez un mammifère, qui comprend: 50
un matériau matriciel spongieux résorbable;
un facteur ostéogénique, ledit facteur ostéogénique étant incorporé dans ledit matériau matriciel spongieux en une quantité qui accélère la vitesse de résorption dudit matériau matriciel spongieux chez un mammifère; et 55

une substance minérale particulaire dont les particules ont un diamètre moyen d'au moins 0,5 mm et qui est encastrée dans ledit matériau matriciel spongieux résorbable, ladite substance minérale particulaire étant utilisée dans une proportion en poids d'au moins 4: 1 par rapport audit matériau matriciel spongieux résorbable de façon à fournir un support pour une croissance interne de la masse osseuse en présence dudit facteur ostéogénique.

2. La composition spongieuse à activité ostéogénique selon la revendication 1, dans laquelle ladite substance minérale particulaire est présente dans une proportion en poids d'au moins 10: 1 par rapport au matériau matriciel spongieux résorbable.
3. La composition spongieuse à activité ostéogénique selon la revendication 1, dans laquelle ledit facteur ostéogénique comprend une protéine morphogénétique osseuse, une protéine de minéralisation LIM ou une séquence nucléotidique codant pour une protéine morphogénétique osseuse ou une protéine de minéralisation LIM.
4. La composition spongieuse à activité ostéogénique selon la revendication 1, dans laquelle ledit matériau matriciel spongieux résorbable contient du collagène.
5. La composition spongieuse à activité ostéogénique selon la revendication 3, dans laquelle ledit matériau matriciel spongieux résorbable contient du collagène.
6. La composition spongieuse à activité ostéogénique selon la revendication 1, dans laquelle ladite substance minérale particulaire est sélectionnée parmi un groupe consistant en des particules osseuses et des céramiques de phosphate de calcium synthétiques biocompatibles.
7. La composition spongieuse à activité ostéogénique selon la revendication 6, dans laquelle ladite substance minérale particulaire comprend du phosphate biphasé de calcium.
8. La composition spongieuse à activité ostéogénique selon la revendication 7, dans laquelle la porosité dudit phosphate biphasé de calcium est de 50 % au moins.
9. La composition spongieuse à activité ostéogénique selon la revendication 8, dans laquelle ladite substance minérale particulaire comprend des particules osseuses.
10. La composition spongieuse à activité ostéogénique

selon la revendication 9, dans laquelle lesdites particules osseuses sont des particules osseuses corticales.

11. La composition spongieuse à activité ostéogénique selon la revendication 1, qui est constituée de 95 % en poids au moins de ladite substance minérale particulaire. 5
12. La composition spongieuse à activité ostéogénique selon la revendication 1, dans laquelle ladite substance minérale particulaire possède des particules de dimensions moyennes comprises entre 0,5 mm et 5,0 mm. 10
13. La composition spongieuse à activité ostéogénique selon la revendication 1, dans laquelle la substance minérale particulaire poreuse possède des particules de dimensions moyennes comprises entre 1 mm et 2 mm. 15
14. La composition spongieuse à activité ostéogénique selon la revendication 1, dans laquelle ledit facteur ostéogénique est une protéine morphogénétique osseuse. 20
15. La composition spongieuse à activité ostéogénique selon la revendication 14, dans laquelle ladite protéine morphogénétique osseuse est une protéine recombinante humaine. 25
16. La composition spongieuse à activité ostéogénique selon la revendication 15, dans laquelle ladite protéine morphogénétique osseuse est BMP-2 ou BMP-7. 30
17. La composition spongieuse à activité ostéogénique selon la revendication 16, qui comprend également un facteur ostéogénique stimulant sélectionné parmi le groupe consistant en un autogreffe de moelle osseuse, un allogreffe de moelle osseuse, le facteur de croissance transformant β , le facteur de croissance fibroblastique, le facteur de croissance dérivé des plaquettes, le facteur de croissance analogue à l'insuline, la β -microglobuline et des stéroïdes. 35
18. Une composition spongieuse à activité ostéogénique efficace dans l'induction d'une croissance osseuse nouvelle chez un primate, comprenant: 40

un matériau matriciel spongieux résorbable;

un facteur ostéogénique qui stimule les ostéoblastes et les ostéoclastes, ledit facteur ostéogénique étant incorporé dans ledit matériau matriciel spongieux en une quantité qui accélère la vitesse de résorption dudit matériau ma-

triciel spongieux chez un primate; et

une substance minérale particulaire dont les particules ont un diamètre moyen d'au moins 0,5 mm et qui est encastrée dans ledit matériau matriciel spongieux résorbable, ladite substance minérale particulaire étant utilisée dans une proportion en poids d'au moins 4: 1 par rapport audit matériau matriciel spongieux résorbable de façon à fournir un support minéral maintenu suffisamment longtemps pour assurer une croissance interne du tissu ostéoïde au niveau du territoire où ladite composition spongieuse est implantée.

19. La composition spongieuse à activité ostéogénique selon la revendication 18, le primate étant un être humain. 15

20. L'utilisation d'une composition ostéogénique spongieuse comprenant: 20

un matériau matriciel spongieux résorbable;

un facteur ostéogénique qui stimule les ostéoblastes et les ostéoclastes, ledit facteur ostéogénique étant incorporé dans ledit matériau matriciel spongieux en une quantité qui accélère la vitesse de résorption dudit matériau matriciel spongieux chez le primate; et 25

une substance minérale particulaire dont les particules ont un diamètre moyen d'au moins 0,5 mm et qui est encastrée dans ledit matériau matriciel spongieux résorbable, ladite substance minérale particulaire étant utilisée dans une proportion en poids d'au moins 4: 1 par rapport audit matériau matriciel spongieux résorbable de façon à fournir un support pour une croissance interne de la masse osseuse en présence dudit facteur ostéogénique; 30

dans la fabrication d'un médicament indiqué dans l'induction de la croissance osseuse chez un primate. 35

21. L'utilisation selon la revendication 20, dans laquelle ladite substance minérale particulaire est présente dans une proportion en poids d'au moins 10: 1 par rapport au matériau matriciel spongieux résorbable. 40

22. L'utilisation selon la revendication 21, dans laquelle ledit facteur ostéogénique comprend une protéine morphogénétique osseuse, une protéine de minéralisation LIM ou une séquence nucléotidique codant pour une protéine morphogénétique osseuse ou une protéine de minéralisation LIM. 45

23. L'utilisation selon la revendication 20, dans laquelle ledit matériau matriciel spongieux résorbable comprend du collagène.
24. L'utilisation selon la revendication 22, dans laquelle ledit matériau matriciel spongieux résorbable comprend du collagène.
25. L'utilisation selon la revendication 20, dans laquelle ladite substance minérale particulaire est sélectionnée parmi le groupe consistant en des particules osseuses, une céramique de phosphate de calcium synthétique biocompatible et des mélanges de ceux-ci.
26. L'utilisation selon la revendication 25, dans laquelle ladite substance minérale particulaire poreuse comprend du phosphate biphasé de calcium.
27. L'utilisation selon la revendication 26, dans laquelle la porosité dudit phosphate biphasé de calcium est de 50 % au moins.
28. L'utilisation selon la revendication 20, dans laquelle ladite substance minérale particulaire comprend des particules osseuses.
29. L'utilisation selon la revendication 28, dans laquelle lesdites particules osseuses sont des particules osseuses corticales.
30. L'utilisation selon la revendication 20, dans laquelle ladite composition spongieuse à activité ostéoinductive est constituée de 95 % en poids au moins de ladite substance minérale particulaire.
31. L'utilisation selon la revendication 20, dans laquelle ladite substance minérale particulaire présente des particules de dimensions moyennes comprises entre 0,5 mm et 5,0 µm.
32. L'utilisation selon la revendication 20, dans laquelle ladite substance minérale particulaire poreuse présente des particules de dimensions moyennes comprises entre 1 mm et 2 mm.
33. L'utilisation selon la revendication 20, dans laquelle ledit facteur ostéogénique est une protéine morphogénétique osseuse.
34. L'utilisation selon la revendication 33, dans laquelle ladite protéine morphogénétique osseuse est une protéine recombinante humaine.
35. L'utilisation selon la revendication 33, dans laquelle ladite protéine morphogénétique osseuse est BMP-2 ou BMP-7.
36. L'utilisation selon la revendication 20, le primate étant un être humain.
37. L'utilisation selon la revendication 20, dans laquelle le territoire concerné est la colonne vertébrale dudit primate.
38. L'utilisation selon la revendication 37, dans laquelle la croissance osseuse est induite pour produire une fusion spinale.
39. L'utilisation selon la revendication 38, dans laquelle ladite fusion spinale est une fusion spinale entre des corps vertébraux.
40. L'utilisation selon la revendication 38, dans laquelle ladite fusion finale est une fusion spinale postéro-latérale.
41. L'utilisation selon la revendication 38, dans laquelle ladite fusion spinale inclut une fusion entre les apophyses transverses de vertèbres adjacentes.
42. Une composition spongieuse à activité ostéogénique pour l'induction d'une croissance osseuse nouvelle chez un primate, comprenant:
- un support consistant essentiellement en une matrice spongieuse résorbable dans laquelle une substance minérale particulaire est encastree, ladite substance minérale particulaire étant présente en une quantité qui correspond à 95 % en poids au moins dudit support; et
- un facteur ostéogénique.
43. Un dispositif spongieux implantable hautement minéralisé consistant essentiellement en une matrice spongieuse résorbable formée de collagène et d'une substance minérale particulaire biocompatible encastree dans ladite matrice, ledit dispositif étant composé de 1 % à 3 % en poids de collagène et de 97 % à 99 % en poids de la substance minérale particulaire biocompatible.
44. Le dispositif selon la revendication 42, dans lequel la substance minérale particulaire biocompatible comprend des particules osseuses.
45. Le dispositif selon la revendication 42, dans lequel la substance minérale particulaire biocompatible comporte une céramique de synthèse.
46. Le dispositif selon la revendication 44, dans lequel le matériau céramique contient une céramique de phosphate de calcium.
47. Le dispositif selon la revendication 45, dans lequel

la céramique de phosphate de calcium correspond au phosphate biphasé de calcium.

48. Un implant ostéogénique comprenant:

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un support matriciel résorbable contenant de 1 % à 3 % en poids de collagène sous une forme spongieuse et de 97 % à 99 % en poids d'une substance minérale particulaire biocompatible encastrée dans ledit collagène; et

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un facteur ostéogénique.

49. Un dispositif de fusion entre les corps vertébraux, comprenant:

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un élément porteur d'une longueur permettant son insertion entre deux vertèbres adjacentes; et

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une composition selon l'une quelconques des revendications 1-19 et 42-48, maintenue par ledit élément porteur.

50. L'utilisation d'un dispositif de fusion entre les corps vertébraux selon la revendication 49 pour la fabrication d'un médicament produisant une fusion des corps vertébraux chez un mammifère.

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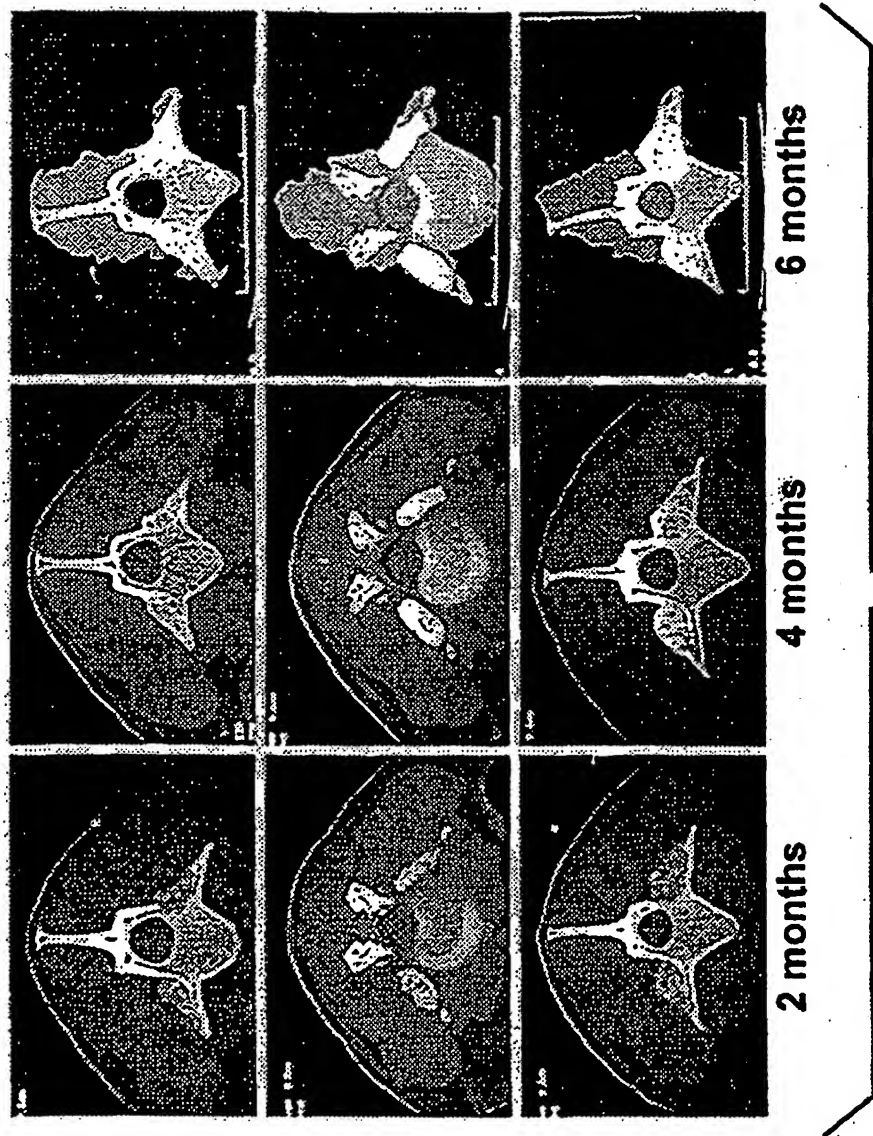


Fig. 1

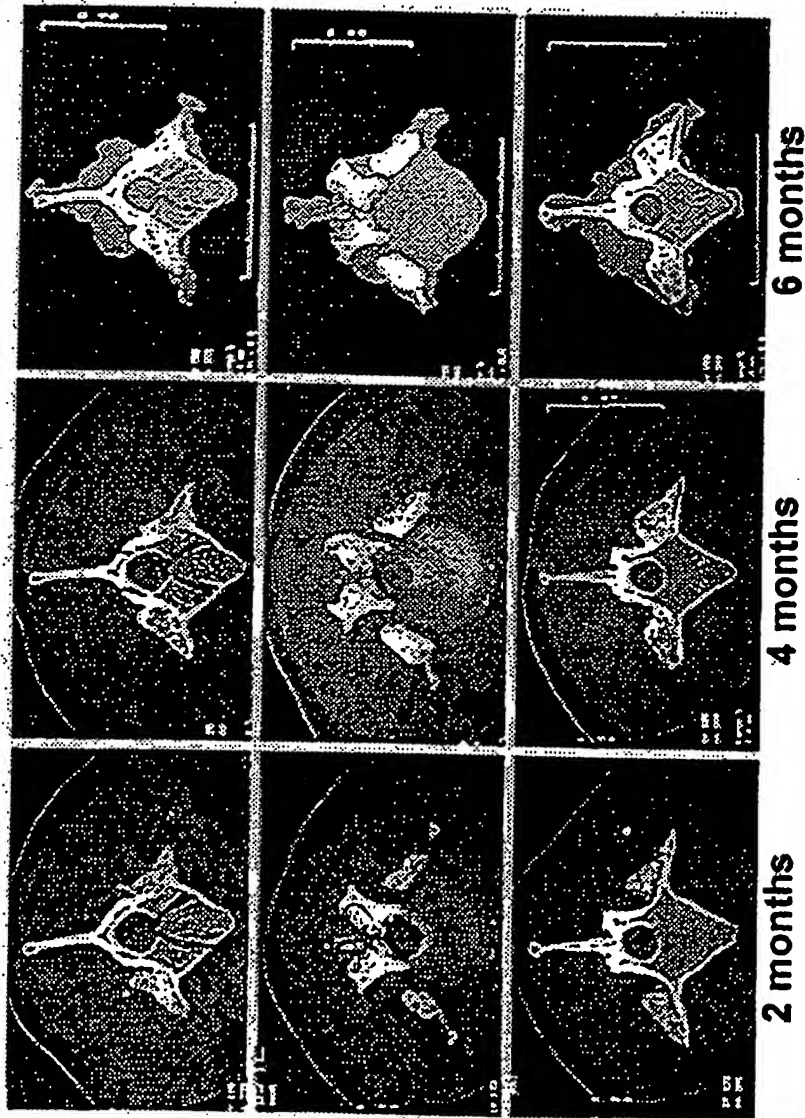


Fig. 2